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Original Article

Phylogenetic and spatial patterns of herbal medicine compounds: Which medicinal plants are phytochemically characterized?

Dacheng Hao [a,1,*], Yaoxuan Wang [a,1], Peigen Xiao [b], Xiaojie Gu [a,*]

[a] Liaoning Provincial Universities Key Laboratory of Environmental Science and Technology, School of Environment and Chemical Engineering, Dalian Jiaotong University, Dalian 116028, China
[b] Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences, Beijing 100193, China

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ABSTRACT

Objective: The study of phytometabolites of medicinal plants and their phylogenetic distribution is an important content of pharmacophylogeny. The objectives of this study were to provide an updated estimate of the extent to which the medicinal plants were investigated phytochemically and relate this to the species-level phylogeny and their geographical pattern.
Methods: Here, we further characterized 1 648 phytometabolites, including terpenoids, steroids, flavonoids, phenylpropanoids, phenolics, alkaloids, etc., reported in journals *Chinese Traditional and Herbal Drugs* (Zhong Cao Yao) and *Chinese Herbal Medicines* (CHM) from the phylogenetic and spatial perspectives. According to the structural characteristics, terpenoids, flavonoids, alkaloids and phenylpropanoids were subdivided into subclasses, and the research effort of phytometabolites was for the first time delineated at both subclass and phylogenetic levels.
Results: The phytometabolites of 90 families were reported on two journals in three years. It is noted that terpenoids with diverse bioactivities still constitute the primary object of phytochemical research, followed by flavonoids, phenolics, phenylpropanoids and alkaloids. Among the reported species, the family Asteraceae had the most, followed by Lamiaceae, Fabaceae, and Ranunculaceae. In the phylogenetic distribution of the reported phytometabolites, the net relatedness index (NRI) results revealed a clustered structure for triterpene, iridoid, flavone, flavonol, coumarin, indole alkaloid and terpenoid alkaloid, while the nearest taxon index (NTI) metric identified the clustered structure for triterpene, sesquiterpene, indole alkaloid and terpenoid alkaloid. Especially in Ranunculaceae, there were more reports on triterpene and terpenoid alkaloid subclasses. The overdispersion pattern of diterpene and phenolic was suggested by NRI and NTI respectively, albeit more reported diterpenes and phenolics were in Lamiaceae. The geographical distribution hotspots of reported species and compounds thereof highlighted the enormous progress of herbal medicine research and industry, which play a positive role in the future drug discovery and development.
Conclusion: These results provide new dimensions and perspectives in the context of pharmacophylogeny for perceiving and evaluating research trends and flashpoints in medicinal phytochemistry.
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1. Introduction

There are currently over 300 000 known plant species, which might produce 200 000 to 1 million metabolites; the medicinal potential of most phytometabolites remains a mystery. Although the phytometabolites of medicinal plants have been widely examined by researchers, there is still an enormous chemical space untapped. Numerous omics studies of medicinal plants were performed to identify biosynthetic pathways of many species and preliminarily establish the links between biosynthetic genes and corresponding phytometabolites, as well as to understand the regulatory mechanisms of environmental stresses, which could enhance the production of useful specialized metabolites. Based on the big data obtained from omics studies, some medicinal plants and their efficacies have been investigated in terms of their phylogenetic distribution (Zaman et al., 2021; Hou et al., 2024). However, what are the possible reasons for the differences in the types of diseases treated by medicinal plants being unevenly distributed on the phylogenetic tree? Can certain patterns exist? Different medicinal taxa produce different combinations of various

* Corresponding authors.
E-mail addresses: hao@djtu.edu.cn (D. Hao), guxiaojie2003@163.com (X. Gu).
[1] These authors have contributed equally to this work.

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medicinal compounds, mainly specialized metabolites; what kind of disease a certain medicinal plant can treat depends on the quality and quantity of the phytometabolites it produces. A few reports about the uneven distribution of phytochemicals on the phylogenetic tree have been published (Defossez et al., 2021; Zhang, Lu, Liu, & Tang, 2021; Zhang et al., 2021a), but much more details about the evolutionary predictability of plant chemodiversity remain unknown, and there is much space to explore.

Unearthing the intricate relationships and connectivity between phylogeny of medicinal plants, their phytometabolites and therapeutic efficacies can be facilitated by pharmacophylogeny studies (Hao & Xiao, 2020a, b), in which the study of chemodiversity and versatility of bioactivities has always been a focus. The last decade has witnessed a keen interest in constructing the large phylogenetic tree (Hu et al., 2020), on which the phytochemical landscape can be mapped, representing a high throughput approach in dealing with large amount of omics information from medicinal plants. Facilitated by the species level phylogeny, it is clear which class/subclass of compounds are shared by which plants, which is conducive to gaining deeper insights from the perspective of pharmacophylogeny. From the year 2021 to 2023, scholars reported a total of 1 648 phytometabolites of angiosperms, including terpenoids, steroids, flavonoids, phenylpropanoids, phenolics, alkaloids (Figs. 1 and 2) and other classes, on journals *Chinese Traditional and Herbal Drugs* (Zhong Cao Yao published in Chinese) and *Chinese Herbal Medicines* (CHM, published in English). Many of them, e.g., turmerone G (Zhang et al., 2023a; Zhang et al., 2023c; Zhang, Lei, Wang, Zhang, & Liu, 2023; Zhang et al., 2023e,b; Zhang et al., 2023d; Zhang, Zhang, Li, Chen, & Chen, 2023), aesculetin (Su et al., 2021), and tribulusimide D (Liu et al., 2023c), are the newly discovered compounds in the specific species/genus between 2021 and 2023, and some of them, e.g., davidioterpene A (Qiu et al., 2023), dalbergipinnatamin A (Wang, Gao, Chen, & Fu, 2023; Wang et al., 2023a), and 3,5-dihydroxy-3′-methoxyflavone-7-*O*-*β*-*D*-glucopyranoside (Wei et al., 2023b), are the compounds with the promising pharmacological effects or the most clinical value. Most reported phytometabolites are from traditional Chinese medicine (TCM) species, illustrating the efficiency of mining chemodiversity from biodiversity of TCM plants. Some phytometabolites have been subjected to the initial pharmacological tests to show their promise in research and industry (Geng, Wang, Wang, & Xiao, 2021; Gong et al., 2022; He, Jiang, Wang, & Li, 2023). These intriguing findings in 2021–2023 inspire researchers in various fields to explore the secret of medicinal plants, and also enable us to continually feel the magic charm of herbal medicine compounds.

Based on the above understanding, we hypothesize that examining the phylogenetic and spatial distribution of medicinal plants and phytometabolites therein could help better characterization and contribute novel awareness about research activities of herbal compounds. Therefore the objectives of this study were to provide an updated estimate of the extent to which the medicinal plants were investigated phytochemically and relate this to the species-level phylogeny and their geographical pattern. Based on the reported phytometabolites of two journals during 2021–2023, we utilized a set of measures to show how research efforts on phytometabolites with medicinal importance are focused.

2. Materials and methods

2.1. Phytometabolite database of reported medicinal plants

The phytometabolite database was firstly digitalized based on phytochemical articles of journals *Chinese Traditional and Herbal Drugs* (Zhong Cao Yao) and *Chinese Herbal Medicines* (CHM) during years 2021–2023 (Bi, Shen, Jiang, Xiao, & He, 2022; Chai et al., 2021; Chen et al., 2023; Chen, Yang, Yang, & Yang, 2023; Chen, Zou, & Chou, 2023), involving 302 species of 231 genera, 91 families (Chen et al., 2021, 2022a). In terms of biosynthetic pathways, all metabolites were classified into seven major categories, i.e., terpenes (Guo et al., 2021; Chen et al., 2022a; Ruan, Lu, Xing, Cui, & Zhao, 2023), alkaloids (Sang et al., 2021; Pan et al., 2022; Li, Fang, Yang, Fang, & Zhou, 2023), flavonoids (Liu, Li, Wang, Zhang, & Liu, 2021; Liu et al., 2021a; Na et al., 2022; Wang, Gao, Chen, & Fu, 2023; Wang et al., 2023a), phenolics (Li et al., 2021a; Shen et al., 2023), phenylpropanoids (Wang, Gao, Chen, & Fu, 2023; Wang et al., 2023b; Yang et al., 2021a), steroids (Li, Fang, Yang, Fang, & Zhou, 2023; Li et al., 2021b; Li et al., 2023a; Zhang et al., 2022a; Zhang & Lu, 2022), and others (Cui et al., 2021; Niu, Luo, Lyu, & Lu, 2021; Yu et al., 2023); the first six classes were subdivided into 35 subclasses (Table S1). The phytometabolite was coded with binary characters: When it is present in a species, it is 1; otherwise, it is 0.

2.2. Phylogenetic tree of medicinal species

The phylogenetic tree full_tree_461.tre (https://www.darwintree.cn/resource/Nature2018/) includes most of China angiosperm species (Hu et al., 2020), i.e. 29 620 species, which was expanded to obtain a larger tree sp_tree_zws.tre, with 30 683 species. A total of 59 species included in our phytometabolite database but not in sp_tree_zws.tre were inserted using *phylo.maker* function of *V.PhyloMaker* package in R 3.5.3 (https://www.r-project.org/), and an expanded phylogenetic tree sp_tree_chm of 30 742 species was obtained. The *phylo.maker* function of *V.PhyloMaker* (Jin & Qian, 2019) makes phylogenetic hypotheses under three scenarios (i.e. scenarios 1–3); only scenario 3, adopted in this study, can match the correct phylogenetic relationship based on the species list used by *V.PhyloMaker*. The single subtree involving phytometabolites of six major classes was extracted from sp_tree_chm.tre; the scientific names of species were mainly based on *Flora of China* (https://www.iplant.cn/frps; FOC). The R packages Picante and Ape (https://cran.r-project.org/web/packages/ape/) were used to generate the subtree. iTOL v6 (https://itol.embl.de/) was used to draw and visualize the subtrees.

2.3. Statistics and calculation of phylogenetic distribution of phytometabolites

Net relatedness index (NRI) measures the extent of deep level (e.g., family/genus) clustering, while nearest taxon index (NTI) calculates the extent of terminal (i.e. species level) lumping (Hao, Zhang, He, & Xiao, 2022). NRI and NTI values were calculated using functions ses.mpd and ses.mntd of Picante package, respectively. The positive values of these two indices suggest the phylogenetic clustering of reported phytometabolite subclass, while negative values indicate that species with the same subclass of phytometabolite are over-dispersed on the phylogenetic tree (Hao, Lyu, Wang, & Xiao, 2023). The observed patterns of phytometabolite distribution were compared with the expected ones to assess whether the values of NRI and NTI were statistically significant ($P < 0.05$). The strength of phylogenetic signal of 35 phytometabolite classes was quantified using D statistic (Hao, Lyu, Wang, & Xiao, 2023), which was implemented by the function phylo.d in R package caper (https://CRAN.R-project.org/package=caper). There was a strong phylogenetic signal when $p(D < 1) < 0.05$ and $p(D > 0) > 0.05$. The phylogenetic diversity (PD) of species with reported phytometabolites was evaluated by PD index, i.e., the total branch length spanned by the phylogenetic tree of these species (Omollo et al., 2024), which was implemented in the function pd of Picante.

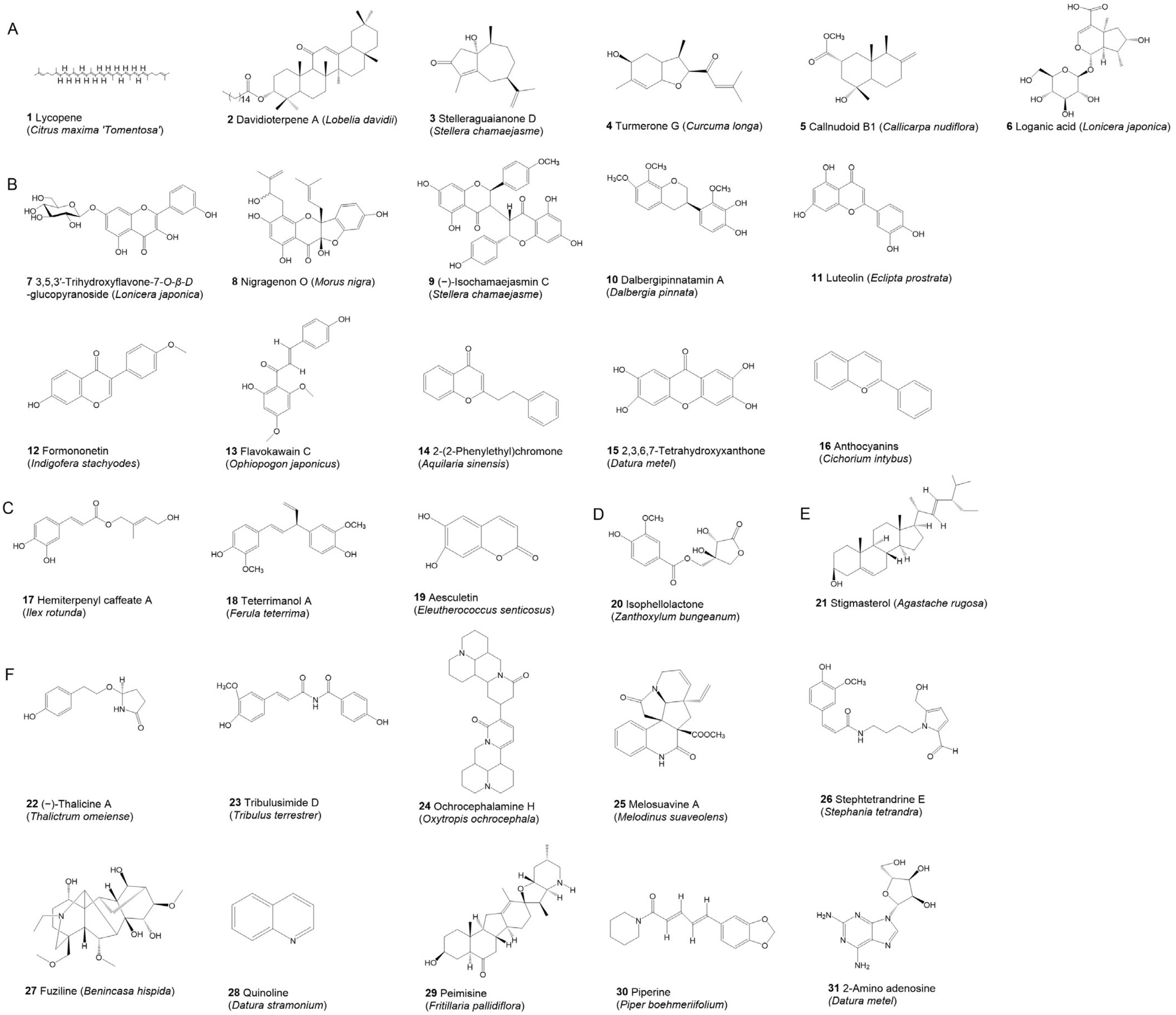

Fig. 1. Examples of chemical structures of reported phytometabolites. One compound was taken from each of 31 subclasses as an example to display. A, Terpenoids **1**–**6** (Chen et al., 2023; Chen, Yang, Yang, & Yang, 2023; Chen, Zou, & Chou, 2023; Qiu et al., 2023; Xu et al., 2021; Zhang et al., 2023a; Zhang et al., 2023c; Zhang, Lei, Wang, Zhang, & Liu, 2023; Zhang et al., 2023e,b; Zhang et al., 2023d; Zhang, Zhang, Li, Chen, & Chen, 2023; Zhou, Liu, Zhou, Chen, & Li, 2023; Zhou et al., 2021c). B, Flavonoids **7**–**16** (Jia, Wang, Jin, Huang, & Hu, 2023; Li et al., 2021b; Liu, Li, Wang, Zhang, & Liu, 2021; Liu et al., 2021a; Wang, Gao, Chen, & Fu, 2023; Wang et al., 2023a; Wei et al., 2023b; Yan et al., 2022; Yan, Zhang, & Liu, 2022; Zhang et al., 2022b; Zhang, Lei, Wang, Zhang, & Liu, 2023; Zhang, Lu, Liu, & Tang, 2021; Zhang et al., 2023a,e; Zhang & Lu, 2022; Zhang et al., 2021b; Zhang, Zhang, Li, Chen, & Chen, 2023; Zhou, Liu, Zhou, Chen, & Li, 2023). C, Phenylpropanoids **17**–**19** (Huang et al., 2023; Su et al., 2021; Zhang, Lei, Wang, Zhang, & Liu, 2023; Zhang et al., 2023e; Zhang, Zhang, Li, Chen, & Chen, 2023). D, Phenolics **20** (Wang, Gao, Chen, & Fu, 2023; Wang et al., 2023d). E, Steroid **21** (Jia, Liu, Huang, Li, & Qian, 2021). F, Alkaloids **22**–**31** (Chen et al., 2023; Chen, Yang, Yang, & Yang, 2023; Chen, Zou, & Chou, 2023; Jin et al., 2021; Li et al., 2023d; Li, Fang, Yang, Fang, & Zhou, 2023; Li et al., 2023b; Li et al., 2023a; Liu et al., 2023c; Liu, Li, Wang, Zhang, & Liu, 2021; Liu et al., 2021a; Qiu et al., 2021; Wang et al., 2023e; Wang, Gao, Chen, & Fu, 2023; Wang et al., 2023f; Wang et al., 2021b; Zhang et al., 2023a; Zhang, Lei, Wang, Zhang, & Liu, 2023; Zhang, Zhang, Li, Chen, & Chen, 2023). The rarely reported subclasses benzoxazine alkaloid, purine alkaloid, imidazole alkaloid, and macrospermine alkaloid are not shown.

2.4. Provincial and county-level geographical distribution of reported medicinal plants and their phytometabolites

The map of China [https://bzdt.ch.mnr.gov.cn/index.html; review drawing number: GS (2019)1822] was utilized; the 753 182 county/district-level occurrence records of 2 305 China plant species (Shan et al., 2022) involve 2 798 county level administrative units, and the occurrence records of 152 out of 296 species included in our phytometabolite database were retrieved. In order to understand the county/district-level distribution of medicinal species and their phytometabolites in 2 789 counties of China, we conducted data mining of occurrence database by writing Python scripts. Two data files, data1 and data2, were introduced. The data1 contained two fields: species name, county name; data2 included species name and names of 35 subclasses. Through merging in terms of field species name, 152 medicinal species and their phytometabolites in our phytometabolite database were matched to the corresponding county. The number of species and compounds of each county was counted. In order to figure out the distribution of medicinal plants and their phytometabolites in 34 provincial level administrative regions of China, we searched FOC to record in which province(s) each of 296 species is distributed.

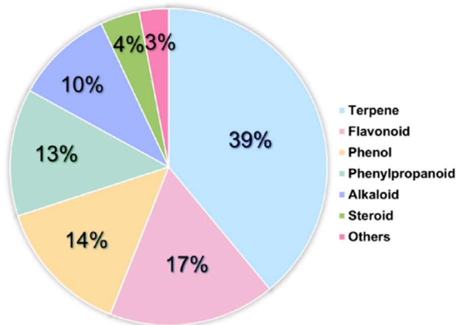

Fig. 2. Pie chart represents proportion of various compounds.

3. Results and discussion

3.1. Phylogenetic distribution of reported medicinal species and phytometabolites

Of reported 302 medicinal species of 91 major medicinal families, 149 species were specifically investigated in terms of their terpenoids (643; Figs. 1, 2 and 3A), followed by 272 flavonoids of 100 species (Fig. 3B), 230 phenolics of 100 species (Fig. 3C), 221 phenylpropanoids of 68 species, 162 alkaloids of 43 species (Fig. 3D) and 66 steroids of 39 species. These medicinal species and their phylogenetically close taxa constitute a vast biologic/-chemical space for bioprospecting (Tables 1 and S1).

A statistically significant clustered structure was suggested by NRI values of > 0 and $P < 0.05$ for seven subclasses (Table 2), includ-

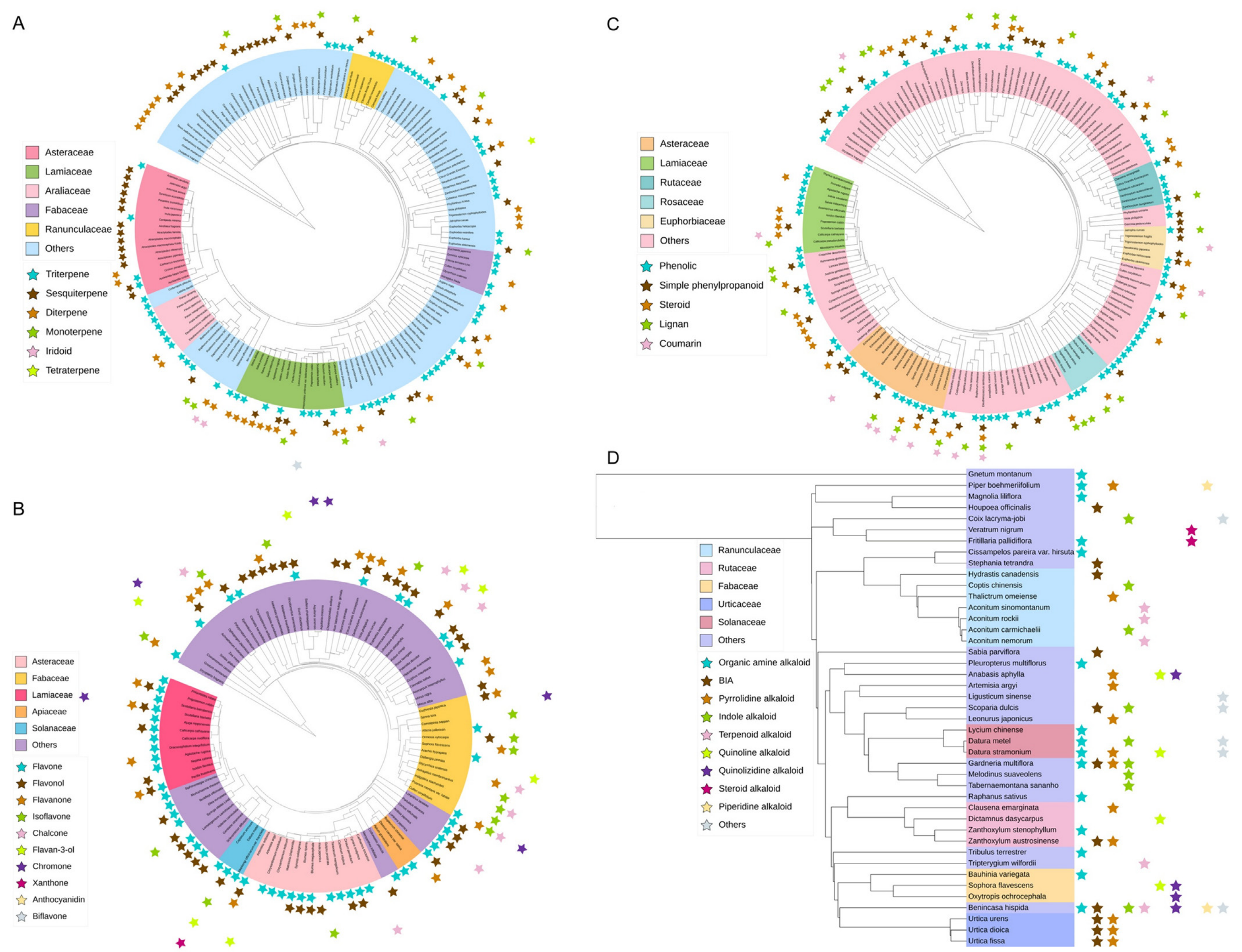

Fig. 3. Distribution of six major classes of reported phytometabolites on the phylogenetic tree of Chinese angiosperms. A, 643 reported terpenoid compounds. There are 149 reported species of 57 medicinal families in this phylogenetic tree. From the inside to the outside of the outer circle are triterpene, sesquiterpene, diterpene, monoterpene, iridoid, tetraterpene. B, 272 reported flavonoid compounds. There are 100 reported species of 44 medicinal families in this phylogenetic tree. From the inside to the outside of the outer circle are flavone, flavonol, flavanone, isoflavone, chalcone, flavan-3-ol, chromone, xanthone, anthocyanidin, biflavone. C, Reported steroid (66), phenylpropanoid (221) and phenolic compounds (230). There are 151 reported species of 71 medicinal families in this phylogenetic tree. From the inside to the outside of the outer circle are phenolic, simple phenylpropanoid, steroid, lignan, coumarin. D, 162 reported alkaloid compounds. There are 43 reported species of 25 medicinal families in this phylogenetic tree.

ing triterpene (Ning, Jia, Wang, & Xu, 2022; Qiu et al., 2023; Yan et al., 2023), iridoid (Long et al., 2021; Wang et al., 2022a; Zhang et al., 2022b; Zhang & Lu, 2022), flavone (Jia, Liu, Huang, Li, & Qian, 2021), flavonol (Luo et al., 2021), coumarin (Wang et al., 2023c; Wu & Xuan, 2021; Zhou et al., 2021a), indole alkaloid (Wu et al., 2023a) and terpenoid alkaloid (Wang et al., 2021a; Han et al., 2022). Seven subclasses, i.e., diterpene (Bu et al., 2022; Chen et al., 2022b), flavanone (Jia, Wang, Jin, Huang, & Hu, 2023; Yuan, Huang, Xiao, Zhang, & Shen, 2021), isoflavone (Du et al., 2021; Zha et al., 2021; Zhang, Lu, Liu, & Tang, 2021; Zhang et al., 2021b), phenolic (Jiang et al., 2023), simple phenylpropanoid (Fang, Fang, & Wang, 2021; Li et al., 2021c; Zhao, Su, Qin, Chang, & Gao, 2022), organic amine alkaloid (Liang, Guo, Hu, & Li, 2023; Liang et al., 2023; Qiu et al., 2021; Wang et al., 2021b) and piperidine alkaloid (Qiu et al., 2021; Zhang et al., 2023a; Zhang et al., 2023c; Zhang, Lei, Wang, Zhang, & Liu, 2023; Zhang et al., 2023e, b; Zhang et al., 2023d; Zhang, Zhang, Li, Chen, & Chen, 2023), were of overdispersion (NRI < 0).

By NTI, the significantly clustered structure was suggested in four subclasses (NTI > 0 and $P < 0.05$), including triterpene (Ma et al., 2022; Yao, Xu, Gong, Zhou, & Luo, 2021; Zhao et al., 2021), sesquiterpene (Li, Fang, Yang, Fang, & Zhou, 2023; Li et al., 2023b; Liu et al., 2021b; Liu, Li, Wang, Zhang, & Liu, 2021; Xiao et al., 2022a), indole alkaloid (Chen et al., 2022c; Yin et al., 2022) and terpenoid alkaloid (Wang et al., 2021a; Han et al., 2022; Yan et al., 2022), which imply that phylogenetically closer species often have analogous subclasses. In Asteraceae, both NRI and NTI suggest triterpene (Liu et al., 2021b; Liu, Li, Wang, Zhang, & Liu, 2021; Liu et al., 2021a; Xu et al., 2021) and steroid (Luo et al., 2021) were of overdispersion, while in Fabaceae, six subclasses, including triterpene, flavone, flavonol, flavanone, chromone and phenolic, were suggested by NRI and NTI to be of overdispersion (Ding et al., 2023; Liang et al., 2021; Long et al., 2022; Tan et al., 2022; Wang et al., 2022b; Yang, Lyu, Xu, Xu, & Zhang, 2022; Zhou et al., 2021b) (Table S2). In Lamiaceae, NRI and NTI suggested the clustering of phenolic (He, Cao, Zeng, Chen, & Zhou, 2021) and diterpene (Bu et al., 2022) respectively, whereas in Ranunculaceae, the clustering of triterpene (Wang et al., 2022c; Xiao et al., 2022b; Zhang, Lu, Liu, & Tang, 2021; Zhang et al., 2021b; Zhang et al., 2021a) and terpenoid alkaloid (Wang et al., 2021a) was implicated.

Overall, values of D statistic suggest the non-stochastic distribution of 12 reported classes of 90 families [$p(D < 1) < 0.05$] (Table S2), such as sesquiterpene (Hu, Dao, & Zhao, 2021; Huang et al., 2021a; Zhang et al., 2023a; Zhang, Lei, Wang, Zhang, & Liu, 2023; Zhang, Zhang, Li, Chen, & Chen, 2023), flavone (Huang et al., 2021b) and benzyltetrahydroisoquinoline alkaloid (BIA) (Chen et al., 2023; Chen, Yang, Yang, & Yang, 2023; Chen, Zou, & Chou, 2023; Zhou et al., 2022). On the other hand, $p(D > 0) < 0.05$ in 13 classes, e.g., monoterpene, simple phenylpropanoid and lignan, suggests that their distribution on the phylogeny was not clumped as significantly as expected by the standard Brownian model of evolution. The results of D statistic largely support those of NRI/NTI and PD. When D statistic was used to investigate the phylogenetic distribution of Asteraceae compounds, it was found

Table 1
Number of phytometabolites in top eight medicinal families.

Families	Top four provinces in China with highest number of metabolites	Terpenes	Flavonoids	Phenols	Steroids	Phenylpropanoids	Alkaloids
Asteraceae	Sichuan, Jiangsu, Jiangxi, Hunan	18	15	12	3	9	1
Lamiaceae	Yunnan, Shannxi, Sichuan, Guangxi	15	12	8	5	2	1
Fabaceae	Guangxi, Yunnan, Guangdong, Guizhou	6	13	4	2	3	3
Ranunculaceae	Hubei, Shannxi, Sichuan, Hunan	6	1	2	2	2	7
Solanaceae	Hebei, Liaoning, Yunnan, Gansu	2	3	2	2	1	3
Apiaceae	Shannxi, Ningxia, Shandong, Hebei	5	3	1	0	2	1
Rutaceae	Guangxi, Jiangxi, Gansu, Shannxi	4	2	5	1	2	4
Euphorbiaceae	Fujian, Guangdong, Guangxi, Guizhou	6	2	3	1	5	0

Table 2
Phylogenetic clustering of reported phytometabolites of 90 medicinal families.

Phytometabolite subclasses	NRI	*P* value	NTI	*P* value	D statistic	*p*(D < 1)	*p*(D > 0)	PD
Triterpene	1.88	0.008*	1.98	0.02*	0.679	0.002*	0*	4 754.0
Sesquiterpene	1.30	0.066	1.60	0.04*	0.618	0*	0.001*	3 589.5
Diterpene	−3.98	1	−0.439	0.662	0.679	0.002*	0*	4 345.8
Monoterpene	0.270	0.638	−0.602	0.738	1.07	0.663	0*	1 700.4
Iridoid	1.09	0.03*	1.73	0.07	0.033	0.022*	0.557	548.1
Flavone	1.84	0.005*	1.50	0.057	0.625	0*	0*	3 827.7
Flavonol	1.64	0.011*	−0.159	0.591	0.720	0.005*	0.001*	3 853.0
Flavanone	−0.990	0.855	0.374	0.358	0.891	0.198	0*	2 377.6
Isoflavone	−1.12	0.786	−0.545	0.709	0.451	0.001*	0.118	1 781.8
Chalcone	0.657	0.155	0.400	0.343	0.603	0.026*	0.114	1 181.7
Flavan-3-ol	0.196	0.584	−0.584	0.733	1.15	0.777	0.004*	1 099.5
Chromone	0.504	0.21	1.51	0.059	0.657	0.062	0.148	852.9
Phenolic	−0.094	0.546	−1.94	0.976	0.907	0.115	0*	7 512.8
Simple phenylpropanoid	−0.455	0.724	−0.758	0.772	1.01	0.552	0*	3 866.9
Steroid	0.809	0.274	0.199	0.437	1.12	0.912	0*	3 425.0
Lignan	0.344	0.526	0.131	0.462	0.870	0.122	0*	2 856.1
Coumarin	1.58	0.002*	1.44	0.071	1.06	0.635	0*	1 290.5
Organic amine alkaloid	−1.31	0.877	−1.60	0.936	0.541	0.005*	0.058	2 055.9
BIA	0.421	0.397	0.672	0.269	0.183	0*	0.362	1 349.6
Pyrrolidine alkaloid	0.652	0.192	0.979	0.16	0.610	0.017*	0.071	1 385.1
Indole alkaloid	0.994	0.041*	1.89	0.022*	0.708	0.061	0.058	950.8
Terpenoid alkaloid	1.30	0.012*	2.39	0.011*	−0.087	0.002*	0.602	650.4
Quinoline alkaloid	0.193	0.475	−0.282	0.625	1.06	0.544	0.071	752.8
Quinolizidine alkaloid	0.598	0.135	0.771	0.206	0.700	0.149	0.21	691.3
Piperidine alkaloid	−0.105	0.924	−0.161	0.942	0.786	0.302	0.313	526.6

Note: *$P < 0.05$, statistically significant.

that sesquiterpene and diterpene were not randomly distributed [$p(D < 1) < 0.05$], and their clustering was as strong as that expected by Brownian model [$p(D > 0) > 0.05$] (Table S2). Triterpene and flavone were of overdispersion in Fabaceae, while triterpene and steroid were of overdispersion in Lamiaceae. Correspondingly, the PD values of most phytometabolite subclasses, especially the high values of phenolic, triterpene and diterpene (Tables 2 and S1), suggest that they span a larger portion of the overall tree, implying the enormous chemical space in the unexplored taxa.

3.2. Provincial and county-level distribution of medicinal plants and phytometabolites

In the FOC based analysis, the top ten families in terms of reported species numbers were widely distributed in various provinces/autonomous regions. Sichuan possessed the most number of reported medicinal species (68) (Fig. 4A, table available upon request), followed by Shaanxi (65) and Guangxi (64). In most provinces, the Asteraceae family had the highest number of reported medicinal species, followed by Lamiaceae and Fabaceae. There were also many phytochemical reports on Ranunculaceae and Solanaceae families. One or several phytometabolites of each medicinal species were reported (Figs. 1 and 3, Table S1), often along with their pharmacological activities (Dong et al., 2023; Dong, Jiang, Wan, & Li, 2023; Liu et al., 2023a; Xu et al., 2023a; Zhang, Lei, Wang, Zhang, & Liu, 2023; Zhang et al., 2023b; Zhang, Zhang, Li, Chen, & Chen, 2023). The top ten phytometabolite subclasses were widely distributed in all provinces/autonomous regions (Fig. 4B, Table S3). The most numerous phytometabolites were identified in Yunnan (249), followed by Guangxi (247) and Sichuan (236). In most provincial administrative units, there were highest number of phenolic compounds, followed by flavone and triterpene (Dong et al., 2023; Dong, Jiang, Wan, & Li, 2023; Xue et al., 2023); the reported sesquiterpene (Wang et al., 2023e; Wang, Gao, Chen, & Fu, 2023; Wang et al., 2023b; Wang et al., 2023f; Wang et al., 2023a; Wang et al., 2023c; Wang et al., 2023d; Zhang et al., 2023c; Zhang, Lei, Wang, Zhang, & Liu, 2023;

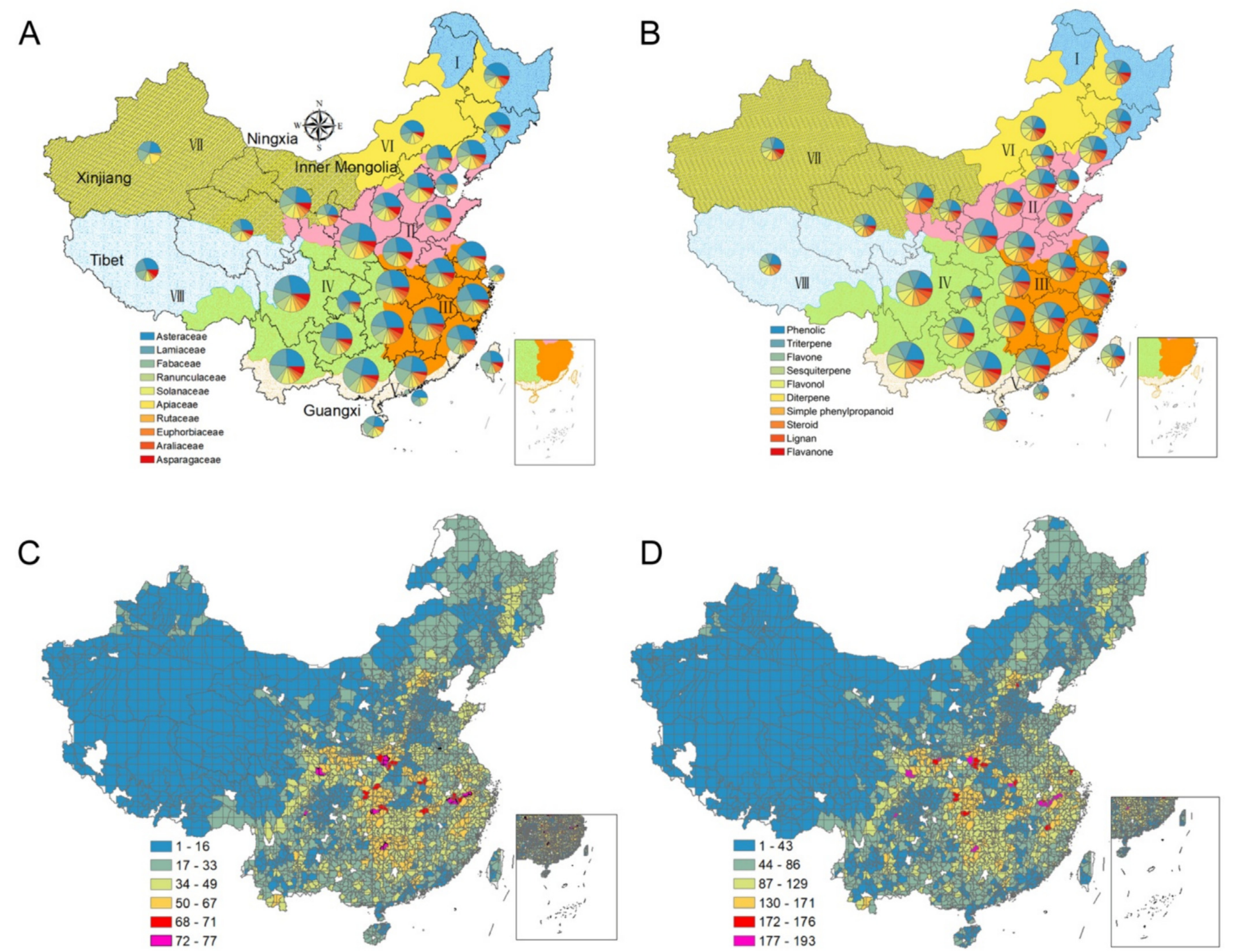

Fig. 4. A, Distribution of top 10 reported medicinal families in China provinces/autonomous regions. The sector area in pie chart represents proportion of reported medicinal species in a certain plant family to total number of medicinal species. The eight major divisions of TCM production are: I, Northeast China; II, North China; III, East China; IV, Southwest China; V, South China; VI, Inner Mongolia; VII, Northwest China; VIII, Qinghai-Tibet Plateau. B, Distribution of top 10 phytometabolite subclasses in provinces/autonomous regions. The sector area in pie chart represents proportion of a certain subclass to total cumulative number of phytometabolite subclasses. The pie size is proportional to number of reported species or cumulative phytometabolite subclasses in each province. C, Distribution of reported species in China counties. The number of species vary between 0 and 77. D, Distribution of reported 35 phytometabolite subclasses in China counties. The number of cumulative phytometabolite subclasses (i.e. a representative compound within same species and phytometabolite subclass is counted as 1) is divided into six levels.

Zhang, Zhang, Li, Chen, & Chen, 2023), flavonol (Wang et al., 2022b) and diterpene (Ge et al., 2023) were also abundant in most provinces.

In county/district level analysis, 35 phytometabolite subclasses of 90 families were widely distributed in 2 789 county level administrative units, spanning all eight major terrestrial TCM production areas (Fig. 4C and D). Gulou District, Nanjing City had the most number of reported medicinal species (77; table available upon request), followed by Xinning County, Hunan Province (76) and Lin'an City, Hangzhou (76), Zhejiang Province. There were also many medicinal species found in counties of provinces such as Sichuan, Gansu, and Anhui, among others. The distribution pattern of six major classes of reported phytometabolites was not significantly different from that of species, and the counties of Gansu, Zhejiang, Jiangsu and some other provinces had the highest number of reported compounds, which agree with distribution patterns and industry planning of commonly used TCM plants in China (Shan et al., 2022, 2023).

Some newly reported phytometabolites have been subjected to the preliminary bioactivity investigations (Li et al., 2023d; Li, Fang, Yang, Fang, & Zhou, 2023; Liang, Guo, Hu, & Li, 2023; Liang et al., 2023; Liu et al., 2023b; Wei et al., 2023a; Zhao et al., 2023a), and their interesting poly-pharmacological properties, such as antitumor (Wei et al., 2023b), anti-oxidant (Liu et al., 2023c; Yang et al., 2023a; Yang, Zhang, Han, Yang, & Wu, 2023), anti-inflammatory (Yang et al., 2023b; Yang, Zhang, Han, Yang, & Wu, 2023; Zhao et al., 2023b), cytotoxic (Kong et al., 2023; Nie et al., 2023), gastroprotective (Chang et al., 2023), tyrosinase inhibitory (Si, Wang, He, Yang, & Huang, 2023), osteoclast inhibitory (Xu et al., 2023b), anti-adipogenic (Yang et al., 2023b; Yang et al., 2023c; Yang et al., 2023a; Yang, Zhang, Han, Yang, & Wu, 2023) and cytoprotective (Dang et al., 2023), warrant further studies. However, the medicinal utility of many more reported compounds is not yet known, such as many of terpene (Cui et al., 2023; Qin, Wu, Yang, Xu, & Hu, 2023), flavonoid (Wu et al., 2023b), alkaloid, phenolic, steroid, phenylpropanoid (Di et al., 2023) and others (Hu et al., 2023; Liu et al., 2023b). With the reference of pharmacophylogeny (Hao & Xiao, 2020a, b), the studies of their pharmacological activities can be more targeted

4. Conclusion

This study inspires and guides researchers, industry insiders in the TCM industry and decision-makers towards a broader herbal landscape. New perspectives in the phylogenetic and spatial distributions of medicinal species and their reported phytometabolites help solve the uncertainty of plant diversity preservation and bioprospecting. The specific patterns of exploring and utilizing botanic resources by the contemporary researchers revealed in the evolutionary and geographic framework could improve our understanding of the intricate relationship between human medicinal culture and ecosystem from the past to the future. Only a limited region of the phytochemical space has been studied (Hou et al., 2024), and focusing on only the primary classification of compounds (Zhang, Lu, Liu, & Tang, 2021; Zhang et al., 2021a) is far from enough. Therefore, this study goes deep into the secondary classification of compounds and sees the feasibility of delving into the tertiary classification of compounds in the future. Some minor subclasses in both southern and northern China have long been less studied, and their importance in sustainable conservation and utilization of medicinal plant diversity is spotlighted here. The continuous accumulation of research data and discoveries in phytochemical space will enrich the conceptual framework of pharmacophylogeny and enhance the foundation of pharmacophylogenomics to better serve humanity and the planet.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Table S1 Phytometabolites of 302 medicinal species reported by journals *Chinese Traditional and Herbal Drugs* (Zhong Cao Yao) and *Chinese Herbal Medicines* (2021–2023). Table S2 Phylogenetic clustering of reported phytometabolites of four major medicinal families. Each sheet displays the calculation results of one family.

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References

Bi, W., Shen, J., Jiang, B., Xiao, P., & He, C. N. (2022). Chemical constituents from leaves of *Acer tataricum* subsp. *ginnala* and their anti-α-glucosidase activities. *Chinese Traditional and Herbal Drugs, 53*(20), 6380–6387.

Bu, L., Peng, C., Liu, F., Meng, C., Guo, L., Zhou, Q., & Xiong, L. (2022). A novel diterpene glycoside from *Leonurus japonicus*. *Chinese Traditional and Herbal Drugs, 53*(1), 8–13.

Chai, L. H., Song, H., Ma, X., Chen, G., Shi, L., & Wei, H. Y. (2021). Study on isolation of chemical constituents from green walnut husks and its antitumor activity *in vitro*. *Chinese Traditional and Herbal Drugs, 52*(19), 5822–5826.

Chang, C., Zhang, H., Ma, J., Huang, H., Wang, Y., Wang, B., ... Li, J. (2023). 2-(2-Phenylethyl) chromones from resinous wood of *Aquilariae Lignum Resinatum* and its gastroprotective effects. *Chinese Traditional and Herbal Drugs, 54*(19), 6208–6213.

Chen, D. L., Ma, G., Liu, H., Wang, C., Yang, Y., Liu, Y., & Wei, J. H. (2023). Two new eudesmane-type sesquiterpenes in "Qi-Nan" agarwood from *Aquilaria sinensis*. *Chinese Traditional and Herbal Drugs, 54*(17), 5135–5141.

Chen, J. G., Yang, Z., Yang, L., & Yang, S. H. (2023). A new aporphine alkaloid from roots of *Stephania tetrandra* and its cytotoxicity. *Chinese Traditional and Herbal Drugs, 54*(1), 41–44.

Chen, J. Y., Ma, G., Qian, F., Sun, L., Li, G., Zhang, L., & Li, Y. M. (2021a). Non-volatile chemical constituents from *Pogostemon cablin*. *Chinese Traditional and Herbal Drugs, 52*(5), 1240–1251.

Chen, L. N., Fu, H., Wang, L., Zhong, L., Yang, J., Xiao, X., ... Luo, Y. H. (2022b). A new labdane diterpene glycoside from stems of *Rubus chingii*. *Chinese Traditional and Herbal Drugs, 53*(10), 2941–2948.

Chen, Q. L., Fan, C., Ao, Y., Sun, B., Ye, W., & Zhang, X. Q. (2022c). Alkaloids from twigs and leaves of *Tabernaemontana sananho*. *Chinese Traditional and Herbal Drugs, 53*(6), 1680–1687.

Chen, Q. Q., Zou, X., & Chou, G. X. (2023). Chemical constituents from *Callicarpae Nudiflorae Folium*. *Chinese Traditional and Herbal Drugs, 54*(1), 15–28.

Cui, X., Zheng, Z., Li, Y., Yu, K., Wang, Y., & Yao, Q. Q. (2021). Chemical constituents from whole herbs of *Viola yedoensis*. *Chinese Traditional and Herbal Drugs, 52*(4), 917–924.

Cui, Y., Wu, J., Qu, C., Li, J., Li, Z., & Liu, Z. (2023). Isolation and identification of two new malonyl ginsenosides from *Panax quinquefolius*. *Chinese Traditional and Herbal Drugs, 54*(21), 6940–6945.

Dang, Z. N., Han, Y., Zhang, Y., Ruan, J., Zhang, Q., Wang, T., & Zhang, Y. (2023). Chemical constituents from vines of *Aspidopterys obcordate*. *Chinese Traditional and Herbal Drugs, 54*(14), 4433–4441.

Defossez, E., Pitteloud, C., Descombes, P., Glauser, G., Allard, P. M., Walker, T. W. N., ... Rasmann, S. (2021). Spatial and evolutionary predictability of phytochemical diversity. *Proceedings of the National Academy of Sciences of the United States of America, 118*(3), e2013.

Di, T. L., Liu, X., Wu, N., Chen, X., Fan, J., & Tan, N. H. (2023). A new dibenzocyclooctadiene lignan from *Schisandra chinensis*. *Chinese Traditional and Herbal Drugs, 54*(12), 3759–3770.

Ding, M. N., Zhou, F., Li, Y., Liu, C., Gu, Y., Wu, J., ... Li, X. (2023). *Cassiae Semen* improves non-alcoholic fatty liver disease through autophagy-related pathway. *Chinese Herbal Medicines, 15*(3), 421–429.

Dong, W. M., Zhu, K., Yang, X., Yin, R., Deng, X., Chen, Z., ... Dong, F. W. (2023). Chemical compositions of the ethyl acetate part from salt-processed *Foeniculi Fructus* and their anti-tyrosinase activities. *Chinese Traditional and Herbal Drugs, 54*(24), 7967–7976.

Dong, X., Jiang, W., Wan, J., & Li, X. H. (2023). Chemical constituents from stems and leaves of *Paris polyphylla* var. *yunnanensis*. *Chinese Traditional and Herbal Drugs, 54*(9), 2705–2709.

Du, K., Tian, M., Sheng, D., Yuan, M., Wang, Y., Li, M., ... Feng, W. S. (2021). A new 6α,11α-dehydropterocarpan from rhizomes of *Pueraria lobata*. *Chinese Traditional and Herbal Drugs, 52*(14), 4130–4135.
Fang, Z. F., Fang, H., & Wang, F. (2021). A new phenylpropanoid from resin of *Styrax tonkinensis*. *Chinese Traditional and Herbal Drugs, 52*(21), 6455–6459.
Ge, W., Chen, J., Li, X., Li, J., Cai, H., Tao, Q., ... Chen, H. J. (2023). Chemical constituents from aerial parts of *Saururus chinensis*. *Chinese Traditional and Herbal Drugs, 54*(11), 3417–3423.
Geng, J. L., Wang, Z., Wang, Q., & Xiao, W. (2021). Chemical constituents from stems and leaves of *Illicium dunnianum*. *Chinese Traditional and Herbal Drugs, 52*(24), 7407–7412.
Gong, S., Cheng, B., Sun, T., Li, X., Liang, X., Wang, Y., ... Xiao, W. L. (2022). Cathayanalactone G and other constituents from leaves and twigs of *Callicarpa cathayana*. *Chinese Herbal Medicines, 14*(2), 332–336.
Guo, Y. Q., Shu, H., Qiao, M., Peng, C., Liu, F., & Xiong, L. (2021). A new seco-bisabolane-type sesquiterpenoid from *Curcuma longa*. *Chinese Traditional and Herbal Drugs, 52*(19), 5814–5818.
Han, M., Wang, T., Shan, L., Chen, L., Huang, S., & Zhou, X. L. (2022). Diterpenoid alkaloids of *Aconitum rockii* and *Aconitum nemorum*. *Chinese Traditional and Herbal Drugs, 53*(12), 3587–3594.
Hao, D. C., Lyu, H. Y., Wang, F., & Xiao, P. G. (2023). Evaluating potentials of species rich taxonomic groups in cosmetics and dermatology: Clustering and dispersion of skin efficacy of Asteraceae and Ranunculales plants on the species phylogenetic tree. *Current Pharmaceutical Biotechnology, 24*(2), 279–298.
Hao, D. C., & Xiao, P. G. (2020a). Pharmaceutical resource discovery from traditional medicinal plants: Pharmacophylogeny and pharmacophylogenomics. *Chinese Herbal Medicines, 12*(2), 104–117.
Hao, D. C., & Xiao, P. G. (2020b). Plant pharmacophylogeny: Past, present and future. *Journal of Chinese Pharmaceutical Sciences, 29*(12), 831–854.
Hao, D. C., Zhang, Y. L., He, C. N., & Xiao, P. G. (2022). Distribution of therapeutic efficacy of Ranunculales plants used by ethnic minorities on the phylogenetic tree of Chinese species. *Evidence Based Complementary and Alternative Medicine, 2022*, 9027727.
He, M. Z., Cao, W., Zeng, G., Chen, Z., & Zhou, Y. J. (2021). Phenolic acids of *Rosmarinus officinalis*. *Chinese Traditional and Herbal Drugs, 52*(13), 3798–3803.
He, Q. H., Jiang, Y., Wang, W., & Li, L. M. (2023). Isolation and identification of alkaloids from *Melodinus magnificus* and their antitumor activity. *Chinese Traditional and Herbal Drugs, 54*(3), 704–710.
Hou, D., Lin, H., Feng, Y., Zhou, K., Li, X., Yang, Y., ... Zeng, X. (2024). CMAUP database update 2024: Extended functional and association information of useful plants for biomedical research. *Nucleic Acids Research, 52*(D1), D1508–D1518.
Hu, L. S., Tan, S., Zhu, Z., Liu, Z., Wu, A., Zhao, Z., & Yang, W. Q. (2023). Study on chemical constituents from stems of *Entada phaseoloides*. *Chinese Traditional and Herbal Drugs, 54*(20), 6596–6602.
Hu, H. H., Liu, B., Liang, Y. S., Ye, J. F., Saqib, S., Meng, Z., ... Chen, Z. D. (2020). An updated Chinese vascular plant tree of life: Phylogenetic diversity hotspots revisited. *Journal of Systematics and Evolution, 58*(5), 663–672.
Hu, Z. Y., Dao, J., & Zhao, M. (2021). A new guaiane sesquiterpene lactone from *Saussurea costus*. *Chinese Traditional and Herbal Drugs, 52*(14), 4136–4140.
Huang, L. Y., Ning, H., Yao, X., Wang, S., Hou, W., & Li, Y. (2021b). Research progress on extraction and purification of luteolin. *Chinese Traditional and Herbal Drugs, 52*(4), 1185–1192.
Huang, W. F., He, J., Zhang, C., He, Y., Wang, B., Lu, M., ... Gao, H. W. (2023). Two new hemiterpenyl caffeates from bark of *Ilex rotunda*. *Chinese Traditional and Herbal Drugs, 54*(8), 2365–2372.
Huang, W. M., Chen, F., Bian, Y., Chen, Z., Shuang, P., Zhou, J., & Luo, Y. M. (2021a). A pair of sesquiterpene enantiomers from *Chloranthus multistachys*. *Chinese Traditional and Herbal Drugs, 52*(4), 925–930.
Jia, A., Wang, L., Jin, J., Huang, C., & Hu, X. (2023). A new sanggenon-type flavanone from *Morus nigra* and its insulin-sensitizing activity. *Chinese Traditional and Herbal Drugs, 54*(1), 45–50.
Jia, R. F., Liu, H., Huang, M., Li, Z., & Qian, S. H. (2021). Chemical constituents from *Agastache rugosa*. *Chinese Traditional and Herbal Drugs, 52*(10), 2884–2889.
Jiang, S. R., Wang, L., Jia, W., Wu, L., Mei, L., Shao, Y., ... Yue, H. L. (2023). Study on phenolic acids and α-glucosidase inhibitory activity of *Nitraria tangutorum* fruit. *Chinese Traditional and Herbal Drugs, 54*(6), 1719–1727.
Jin, Y., & Qian, H. (2019). V. PhyloMaker: An R package that can generate very large phylogenies for vascular plants. *Ecography, 42*, 1353–1359.
Jin, Y. X., Wei, H., Ma, X., Chen, G., Shi, L., & Zhang, J. (2021). Chemical constituents from *Fritillaria palldiflora* and their antitumor activities *in vitro*. *Chinese Traditional and Herbal Drugs, 52*(6), 1562–1567.
Kong, L. T., Zhao, C., Xia, L., Jia, X., Bai, Z., & Tang, W. Z. (2023). Alkaloids from stem barks of *Magnolia liliflora*. *Chinese Traditional and Herbal Drugs, 54*(20), 6587–6591.
Li, C. L., Meng, X., Shang, X., Zhao, Y., & Yang, J. L. (2021a). Constituents of *Zanthoxylum bungeanum* pericarps and their anti-oxidative activity. *Chinese Traditional and Herbal Drugs, 52*(10), 2869–2875.
Li, M. X., Cui, X., Huang, D., Ji, R., Yang, J., & He, X. (2023d). Chemical constituents from *Tripterygium wilfordii* and antioxidant activities of flavanols. *Chinese Traditional and Herbal Drugs, 54*(19), 6220–6227.
Li, R., Fang, Z., Yang, Z., Fang, L., & Zhou, J. (2023). Chemical constituents of alkaloids from *Melodinus suaveolens*. *Chinese Traditional and Herbal Drugs, 54*(5), 1362–1369.
Li, X. H., Yuan, M., Lu, X., Li, L., Li, Z., Mei, S., ... Dong, X. (2021b). Study on chemical constituents of *Ophiopogon japonicus*. *Chinese Traditional and Herbal Drugs, 52*(13), 3804–3809.
Li, Y. P., Lou, S., Yang, R., Zhang, L., Zou, Q., Shang, S., ... Wang, W. G. (2023b). Cytotoxic sesquiterpene aryl esters from *Armillaria gallica* 012m. *Chinese Herbal Medicines, 15*(2), 343–346.
Li, Y. Z., Zhang, D., Jiang, Y., Deng, C., Wang, W., Liu, J., & Song, X. M. (2023a). Two new steroidal constituents from roots and rhizomes of *Helleborus thibetanus*. *Chinese Traditional and Herbal Drugs, 54*(15), 4769–4773.
Liang, G. Y., Guo, X., Hu, J., & Li, J. Y. (2023). A new glucosyloxybenzyl derivative from *Bletilla ochracea* and their procoagulant activity. *Chinese Traditional and Herbal Drugs, 54*(20), 6580–6586.
Liang, M., Wang, Y., Li, X., He, R., Xie, T., Yang, B., ... Huang, Y. L. (2023). Chemical constituents from *Bauhinia variegate*. *Chinese Traditional and Herbal Drugs, 54*(14), 4427–4432.
Liang, X. L., Ji, M., Chen, L., Liao, Y., Kong, X., Xu, X., ... Wilson, D. (2021). Traditional Chinese herbal medicine *Astragalus Radix* and its effects on intestinal absorption of aconite alkaloids in rats. *Chinese Herbal Medicines, 13*(2), 235–242.
Liu, C., Sun, Z., Abulizi, X., Ma, G., Shi, L., & Zhang, J. (2023b). Study on chemical composition of *Hyssopus cuspidatus*. *Chinese Traditional and Herbal Drugs, 54*(18), 5481–5486.
Liu, J., Zhang, H., Han, Y., Lin, C., Zhang, T., & Zou, Z. M. (2023a). Chemical constituents and biological activities of xanthones from *Canscora lucidissima*. *Chinese Traditional and Herbal Drugs, 54*(23), 7723–7729.
Liu, L., Ni, H., Qiu, X., Zhu, L., Wang, H., Tan, Y., ... Zhao, M. (2021b). A new eudesmane sesquiterpene lactone from *Inula racemose*. *Chinese Traditional and Herbal Drugs, 52*(12), 3475–3479.
Liu, X. M., Zhao, J., Lan, J., Wei, J., Cheng, Z., Mei, H., ... Ding, J. H. (2023c). Chemical constituents from fruits of *Tribulus terrestrer* and their antioxidant activity. *Chinese Traditional and Herbal Drugs, 54*(15), 4774–4779.
Liu, X. N., Li, H., Wang, S., Zhang, J., & Liu, D. (2021). Sesquiterpene lactones of *Aucklandia lappa*: Pharmacology, pharmacokinetics, toxicity, and structure–activity relationship. *Chinese Herbal Medicines, 13*(2), 167–176.
Liu, Y., Rong, X., Tan, J., Pan, J., Guan, W., Kuang, H., & Yang, B. Y. (2021a). Chemical constituents of flavonoids and alkaloids from leaves of *Datura metel*. *Chinese Traditional and Herbal Drugs, 52*(14), 4141–4152.
Long, G. Q., Wang, D., Hu, G., Wei, J., Wang, A., & Jia, J. M. (2022). Chemical constituents of *Sophora flavescens* and its antitumor activities *in vitro*. *Chinese Traditional and Herbal Drugs, 53*(4), 978–984.
Long, Z. H., Wang, Q., Li, B., Zhang, Y., Jia, Q., Li, Y., & Zhu, W. L. (2021). A new iridoid glycoside from *Buddleja officinalis*. *Chinese Traditional and Herbal Drugs, 52*(1), 35–44.
Luo, W., Tang, L., Yuan, J., Kang, Q., Li, L., & Chen, H. L. (2021). Chemical constituents of *Cirsium pendulum*. *Chinese Traditional and Herbal Drugs, 52*(22), 6781–6789.
Ma, L., Wang, J., Chai, T., Wang, C., Meng, X., & Yang, J. L. (2022). New triterpenes from roots of *Euphorbia kansui* and their antioxidant activities. *Chinese Traditional and Herbal Drugs, 53*(8), 2269–2273.
Na, H. Y., Zhang, X., Chen, Y., Li, P., Liang, G., & Hua, H. M. (2022). A new flavonoid glycoside isolated from medicinal *Hippophae rhamnoides* juice. *Chinese Traditional and Herbal Drugs, 53*(3), 659–666.
Nie, C. D., Sha, D., He, X., He, B., Tian, Y., Liu, Y., ... Wen, J. (2023). Study on chemical constituents from *Forsythia suspensa*. *Chinese Traditional and Herbal Drugs, 54*(17), 5487–5497.
Ning, R. N., Jia, D., Wang, X., & Xu, J. Q. (2022). A new friedelane triterpene from *Celastrus monospermus*. *Chinese Traditional and Herbal Drugs, 53*(2), 342–346.
Niu, X. N., Luo, W., Lyu, C., & Lu, J. C. (2021). A new polyacetylene from wild ginseng. *Chinese Traditional and Herbal Drugs, 52*(1), 23–27.
Omollo, W. O., Rabarijaona, R. N., Ranaivoson, R. M., Rakotoarinivo, M., Barrett, R. L., Zhang, Q., ... Lu, L. M. (2024). Spatial heterogeneity of neo- and paleo-endemism for plants in Madagascar. *Current Biology, 34*(6), 1271–1283.
Pan, R. Y., Sun, Y., Chen, H., Li, M., Si, Y., & Feng, W. S. (2022). Terpenoids and alkaloids from *Cissampelos pareira* var. *hirsute*. *Chinese Traditional and Herbal Drugs, 53*(18), 5607–5612.
Qin, S. H., Wu, S., Yang, L., Xu, F., & Hu, J. M. (2023). Chemical composition of flower stem of *Gastrodia elata*. *Chinese Traditional and Herbal Drugs, 54*(23), 7717–7722.
Qiu, J. L., Chen, J., Wei, Y., Wang, Z., Li, H., Fu, M., ... Gu, W. (2023). A new triterpenoids and biological activities from *Lobelia davidii*. *Chinese Traditional and Herbal Drugs, 54*(6), 1713–1718.
Qiu, X., Wang, W., Wang, F., Jiang, X., Wei, G., & Li, X. M. (2021). A novel nitrogen-bearing lignan from *Piper boehmeriifolium*. *Chinese Traditional and Herbal Drugs, 52*(18), 5483–5488.
Ruan, Q. F., Lu, Q., Xing, D., Cui, H., & Zhao, Z. X. (2023). A new sesquiterpenoid from roots of *Lindera glauca*. *Chinese Traditional and Herbal Drugs, 54*(2), 457–464.
Sang, C. C., Li, Z., Pang, X., Zou, X., Ye, W., & Zhang, X. Q. (2021). Alkaloid constituents from twigs and leaves of *Gardneria multiflora*. *Chinese Traditional and Herbal Drugs, 52*(8), 2210–2216.
Shan, Z. J., Ye, J. F., Hao, D. C., Xiao, P. G., Chen, Z. D., & Lu, A. M. (2022). Distribution patterns and industry planning of commonly used traditional Chinese medicinal plants in China. *Plant Diversity, 44*(3), 255–261.
Shan, Z. J., Zhang, Q., Qi, Y. D., Ye, J. F., Hao, D. C., Xiao, P. G., ... Chen, Z. D. (2023). Production regionalization of commonly used medicinal plants in China based on botanical big data. *Industrial Crops and Products, 202*, 117024.

Shen, L., Li, X., Cao, L., Wang, Z., Xiao, W., & Geng, J. L. (2023). A new phenolic acid from leaves of *Illicium dunnianum*. *Chinese Traditional and Herbal Drugs, 54*(20), 6592–6595.

Si, X. Y., Wang, Y., He, R., Yang, B., & Huang, Y. L. (2023). Chemical constituents from leaves of *Castanopsis lamontii* and its tyrosinase inhibitory activities. *Chinese Traditional and Herbal Drugs, 54*(19), 6214–6219.

Su, J., Feng, Y., Lin, B., Li, Y., Huang, W., & Wang, Q. (2021). Isolation and identification of chemical constituents from *Acanthopanax senticosus*. *Chinese Traditional and Herbal Drugs, 52*(16), 4783–4788.

Tan, S. L., Yi, T., Yang, W., Jiang, S., Zhang, D., Cui, H., & Zhao, Z. X. (2022). A new cinnamylphenol from stems of *Dalbergia pinnata*. *Chinese Traditional and Herbal Drugs, 53*(8), 2274–2277.

Wang, F., Zhang, J., Li, Y., Zhang, D., Zhang, H., Huang, W., ... Song, X. M. (2021a). One new diterpenoid alkaloid from *Aconitum sinomontanum*. *Chinese Traditional and Herbal Drugs, 52*(3), 626–629.

Wang, J., Zhang, H., Zhu, W., Peng, Y., Xue, C., Chen, Z., ... Hua, H. M. (2023e). Study on chemical constituents of *Thalictrum omeiense*. *Chinese Traditional and Herbal Drugs, 54*(7), 2028–2035.

Wang, J. B., Gao, C., Chen, H., & Fu, H. Z. (2023). A new sesquiterpenoid from *Teucrium viscidum*. *Chinese Traditional and Herbal Drugs, 54*(24), 7953–7958.

Wang, J. L., Zhang, W., Shang, Y., Li, W., Tang, L., Zhu, Y., ... Su, Y. F. (2023b). A pair of new lignan glycosides from Tibetan medicine *Lancea tibetica*. *Chinese Traditional and Herbal Drugs, 54*(10), 3049–3053.

Wang, K., Liu, S., Li, M., Li, L., Yu, J., & Wang, X. (2022a). Chemical constituents from *Lonicera japonica* leaves and their hepatoprotective activities. *Chinese Traditional and Herbal Drugs, 53*(8), 2285–2291.

Wang, Q., Chen, X., Ruan, S., Yan, W., Ni, L., Zou, S., & Zou, X. X. (2022b). A new lignan from leaves of *Ormosia xylocarpa*. *Chinese Traditional and Herbal Drugs, 53*(3), 653–658.

Wang, T. T., Zhang, Y., Zhang, H., Xue, Z., Huo, X., Zeng, Y., & Tan, C. J. (2023f). A new quinolizidine alkaloid from *Oxytropis ochrocephala*. *Chinese Traditional and Herbal Drugs, 54*(4), 1026–1032.

Wang, W. Y., He, H., Zhu, M., Ning, X., Qin, C., Lu, C., ... Wei, J. H. (2023a). A pair of new isoflavan enantiomers from Zhuang medicine *Dalbergia pinnata*. *Chinese Traditional and Herbal Drugs, 54*(7), 2021–2027.

Wang, X. Y., Li, H., Lu, Y., Ping, Y., Zhang, Y., & Tang, H. F. (2022c). Triterpenoid saponins from aerial parts of *Anemone taipaiensis*. *Chinese Traditional and Herbal Drugs, 53*(16), 4925–4933.

Wang, Y., Shi, F., Lu, Z., Zhang, M., Zhang, Z., Jia, F., ... Shi, S. P. (2023c). Seven new 3,4-dihydro-furanocoumarin derivatives from *Angelica dahurica*. *Chinese Herbal Medicines, 15*(3), 457–462.

Wang, Y. P., Shi, B., Liu, J., Chen, L., Huang, S., Zhao, L., & Zhou, X. L. (2023d). Chemical constituents of *n*-butanol fraction of pericarps of *Zanthoxylum bungeanum*. *Chinese Traditional and Herbal Drugs, 54*(5), 1353–1361.

Wang, Y. W., He, J., Wang, X., Gan, H., Zhang, W., & Xu, J. K. (2021b). Alkaloid composition of *Datura metel*. *Chinese Traditional and Herbal Drugs, 52*(20), 6163–6167.

Wei, X. F., Shen, W., Li, Y., Xie, Q., Tang, X., & Ge, L. L. (2023b). Flavonoid glycosides of *Lonicera japonica* flower buds. *Chinese Traditional and Herbal Drugs, 54*(11), 3424–3429.

Wei, Y., Dong, W., Li, W., Zeng, J., Chen, H., Yuan, J., ... Guo, Z. (2023a). Two 2-(2-phenylethyl) chromone dimers with α-glucosidase inhibitory activity from agarwood of *Aquilaria filaria*. *Chinese Traditional and Herbal Drugs, 54*(22), 7336–7341.

Wu, H., Song, J., Fan, K., Qin, M., Hu, W., Guo, R., ... Ding, C. F. (2023a). Indole alkaloids from roots of *Rauvolfia yunnanensis* and its antibacterial activities. *Chinese Traditional and Herbal Drugs, 54*(4), 1033–1042.

Wu, R. F., & Xuan, L. J. (2021). Two new coumarins from fruit of *Garcinia pedunculata*. *Chinese Traditional and Herbal Drugs, 52*(6), 1549–1554.

Wu, Y. Q., Yan, B., Ruan, L., Yao, C., Liu, X., Song, M., ... Song, Z. J. (2023b). Study on flavonoids and flavonoid glycosides from *Desmodium styracifolium*. *Chinese Traditional and Herbal Drugs, 54*(15), 4780–4788.

Xiao, H., Guo, Y., Li, Z., Sun, S., Wang, H., Lyu, C., ... Wang, W. (2022b). Chemical constituents from aerial parts of *Clematis manshurica* (II). *Chinese Traditional and Herbal Drugs, 53*(16), 4934–4939.

Xiao, Y. Z., Muhammad, I., Ma, X., Yu, H., Yan, S., Xiao, X., & Jin, H. Z. (2022a). Camganoids A and B, two new sesquiterpenes with different carbon skeletons isolated from fruits of *Cinnamomum migao*. *Chinese Herbal Medicines, 14*(4), 638–642.

Xu, F. F., Du, H., Zhang, X., Li, Z., Xu, B., Zhu, W., ... Xiao, W. (2021). Online mid-infrared spectroscopy for monitoring seven index components in alcohol precipitation process of *Lonicerae Japonicae Flos* and *Artemisiae Annuae Herba* of Reduning Injection. *Chinese Traditional and Herbal Drugs, 52*(10), 2909–2917.

Xu, L. L., Chen, Z., He, M., Yang, B., Fu, J., Chen, F., & Luo, Y. M. (2023b). A new norditerpenoid from gum resin of *Boswellia carterii*. *Chinese Traditional and Herbal Drugs, 54*(18), 5833–5839.

Xu, R. W., Fan, Y., Zhu, Y., Zhang, X., Xue, G., Zeng, M., ... Chen, H. (2023a). Chemical constituents from *Piperis Kadsurae Caulis* and their neuroprotective activities. *Chinese Traditional and Herbal Drugs, 54*(24), 7959–7966.

Xue, T. T., Tang, Z., Duan, J., Ruan, K., Yang, Y., Song, Z., & Xu, H. B. (2023). Chemical constituents from arial part of *Althaea officinalis* and their inhibition activities *in vitro* toward α-glucosidase and 5-lipoxygenase. *Chinese Traditional and Herbal Drugs, 54*(10), 3060–3070.

Yan, H. J., Chen, Y., Lin, Y., Li, E., Duan, W., & Geng, Y. (2023). A new triterpenoid from leaves of *Dysoxylum binectariferum*. *Chinese Traditional and Herbal Drugs, 54*(22), 7331–7335.

Yan, J. G., Wang, Y., Wu, X., Chen, M., Zheng, Y., Wang, Y., & Ma, S. C. (2022). Chemical constituents of sesquiterpene alkaloids from *Tripterygium wilfordii*. *Chinese Traditional and Herbal Drugs, 53*(7), 1933–1938.

Yan, M., Zhang, Z., & Liu, Y. (2022). Difference analysis of different parts of chicory based on HPLC fingerprint and multi-component content determination. *Chinese Herbal Medicines, 14*(2), 317–323.

Yang, G., Cui, X., Zhang, J., Chen, T., Liu, Y., & Wang, Y. F. (2023b). Chemical constituents from *Elsholtzia bodinieri* and their anti-inflammatory activities. *Chinese Traditional and Herbal Drugs, 54*(12), 3777–3784.

Yang, G. D., Liu, Y., Liu, Y., Ma, Y., Li, Y., & Chen, J. (2023c). Chemical constituents from ethyl acetate extract of *Callicarpa nudiflora* and its anti-inflammatory activity. *Chinese Traditional and Herbal Drugs, 54*(16), 5146–5153.

Yang, J. B., Gao, H., Wang, X., Song, Y., Duan, B., Cheng, X., ... Ma, S. C. (2021a). A new lignanamide isolated from roots of *Polygonum multiflorum*. *Chinese Traditional and Herbal Drugs, 52*(18), 5475–5482.

Yang, L. Y., Wang, C., Chen, J., Qiu, J., Du, C., Wei, Y., ... Gu, W. (2023a). Chemical constituents and bioactivitie of whole plant of *Primulina eburnea* from Guizhou. *Chinese Traditional and Herbal Drugs, 54*(11), 3430–3437.

Yang, P. W., Zhang, P., Han, Z., Yang, Y., & Wu, T. (2023). Two new sulfur−containing derivatives from *Raphani Semen*. *Chinese Traditional and Herbal Drugs, 54*(11), 3408–3416.

Yang, X. W., Lyu, Q., Xu, Q., Xu, W., & Zhang, Y. T. (2022). Study on chemical constituents from cyclohexane soluble part of *Psoraleae Fructus*. *Chinese Traditional and Herbal Drugs, 53*(11), 3269–3279.

Yao, C. H., Xu, X., Gong, X., Zhou, X., & Luo, Z. L. (2021). Cucurbitane triterpenes from *Hemsleya pengxianensis* and their antitumor activity. *Chinese Traditional and Herbal Drugs, 52*(20), 6144–6151.

Yin, X., Zhu, W., Zhou, Y., Wei, X., Hu, R., Zhou, Y., & Feng, T. T. (2022). A new alkaloid from seeds of *Coix lacryma-jobi*. *Chinese Traditional and Herbal Drugs, 53*(10), 2937–2940.

Yu, L., Zhao, M., Dong, L., Huang, Z., Ji, M., Cao, M., ... Zhang, X. P. (2023). Chemical constituents from *Spiranthes sinensis*. *Chinese Traditional and Herbal Drugs, 54*(13), 4089–4095.

Yuan, W. L., Huang, Z., Xiao, S., Zhang, W., & Shen, Y. (2021). Acute toxicity study of flavonoids from *Sophorae Tonkinensis Radix* et *Rhizoma* on zebrafish. *Chinese Traditional and Herbal Drugs, 52*(10), 2978–2986.

Zaman, W., Ye, J. F., Saqib, S., Liu, Y., Shan, Z., Hao, D. C., & Xiao, P. G. (2021). Predicting potential medicinal plants with phylogenetic topology: Inspiration from the research of traditional Chinese medicine. *Journal of Ethnopharmacology, 281*, 114515.

Zha, X. J., Shi, Q., Shao, F., Zhang, P., Liu, R., Yang, M., & Rao, Q. R. (2021). Chemical constituents of *Euphorbia helioscopia*. *Chinese Traditional and Herbal Drugs, 52*(2), 341–348.

Zhang, D. D., Fan, H., Sun, Y., Zhang, H., Jiang, Y., Li, Y., ... Song, X. M. (2022b). A new monoepoxylignan from *Valeriana officinalis*. *Chinese Traditional and Herbal Drugs, 53*(1), 25–30.

Zhang, J., Ma, X., Wang, W., Wu, X., Ma, B., Yu, C., & Wang, H. F. (2023a). Three new sesquiterpenes from roots of *Curcuma longa*. *Chinese Herbal Medicines, 15*(3), 470–474.

Zhang, L. D., Long, Y., Wang, R., Cao, Y., Fan, X., Zou, K., & Wang, H. (2023c). A new furanosesquiterpenoid from *Ranunculi Ternati Radix*. *Chinese Traditional and Herbal Drugs, 54*(14), 4413–4419.

Zhang, M., Lei, J., Wang, Y., Zhang, J., & Liu, D. (2023). Ethnopharmacology, phytochemistry and pharmacology of *Benincasae Exocarpium*: A review. *Chinese Herbal Medicines, 15*(1), 15–26.

Zhang, Q., Lu, Y., Liu, Y., & Tang, H. F. (2021). Chemical constituents of *n*-BuOH fraction from ethanolic extract of *Clematis heracleifolia*. *Chinese Traditional and Herbal Drugs, 52*(17), 5185–5191.

Zhang, X., Li, M., Wang, Y., Chen, Q., Liu, J., Li, S., & Tang, S. A. (2023e). Study on chemical constituents from *Ferula teterrima*. *Chinese Traditional and Herbal Drugs, 54*(8), 2373–2378.

Zhang, X., Liu, Y., Li, Y., Zhang, D., Jiang, Y., Song, X., ... Deng, C. (2022a). Two new steroidal saponins from the roots and rhizomes of *Maianthemum henryi*. *Chinese Traditional and Herbal Drugs, 53*(20), 6375–6379.

Zhang, X., Xie, Y., Liu, Q., Guan, Y., Zhao, S., Liu, Q., ... Guo, D. X. (2023b). Diterpenoids and their anti-inflammatory activities of *Acanthopanacis Cortex*. *Chinese Traditional and Herbal Drugs, 54*(23), 7709–7716.

Zhang, X. C., & Lu, C. H. (2022). Chemical constituents from whole herbs of *Eclipta prostrata* and active components inhibit T3SS of Salmonella. *Chinese Traditional and Herbal Drugs, 53*(16), 4940–4947.

Zhang, Y., Meng, H., Lyu, F., Fan, X., Liu, P., He, X., & Wei, J. (2023d). Temporal characteristics of agarwood formation in *Aquilaria sinensis* after applying whole-tree agarwood-inducing technique. *Chinese Herbal Medicines, 15*(1), 37–44.

Zhang, Y. F., Zan, N., Zhu, Z., Wang, W., Liu, L., Zhang, S., ... Li, J. (2021b). Flavonoids from roots of Miao medicine *Indigofera stachyodes*. *Chinese Traditional and Herbal Drugs, 52*(12), 3485–3492.

Zhang, Y. Y., Zhang, X., Li, W., Chen, S., & Chen, J. (2023). Three new bisabolene-type sesquiterpenoid from *Curcuma longa*. *Chinese Traditional and Herbal Drugs, 54*(14), 4420–4426.

Zhang, Y. Z., Deng, T., Sun, L., Landis, J. B., Moore, M. J., Wang, H., ... Sun, H. (2021a). Phylogenetic patterns suggest frequent multiple origins of secondary metabolites across the seed-plant 'tree of life'. *National Science Review, 8*(4), nwaa105.

Zhao, P. A., Mahesuti, L., Ma, G., Sun, Z., Xu, X., Shi, L., & Gao, X. (2023b). Chemical constituents of *Nepeta bracteata* and its anti-inflammatory activities. *Chinese Traditional and Herbal Drugs, 54*(22), 7342–7350.

Zhao, W. Y., Su, Y., Qin, T., Chang, Y., & Gao, X. M. (2022). Two new phenylpropanoid glycosides from rhizoma of *Phragmites communis*. *Chinese Traditional and Herbal Drugs, 53*(19), 5955–5958.

Zhao, X., Liu, H., Wang, H., Lin, K., Li, J., Pan, W., ... Sun, C. (2023a). One new lignan glucoside from *Callicarpa pseudorubella*. *Chinese Traditional and Herbal Drugs, 54*(21), 6953–6960.

Zhao, Y. N., Zhao, M., Li, J., Shi, Z., Wang, J., Wang, D., ... Zhang, S. J. (2021). A new nortriterpene from barks of *Betula platyphylla*. *Chinese Traditional and Herbal Drugs, 52*(20), 6152–6156.

Zhou, D., Liu, L., Zhou, G., Chen, G., & Li, N. (2023). Chemical constituents from *Stellera chamaejasme*. *Chinese Traditional and Herbal Drugs, 54*(1), 29–34.

Zhou, H. Z., Luo, W., Chen, S., Chen, H., Li, G., & Li, L. M. (2021a). Coumarins from flowers of *Stellera chamaejasme* and their biological activities. *Chinese Traditional and Herbal Drugs, 52*(4), 943–950.

Zhou, Q., Du, W., Li, Z., Wang, Q., Li, Y., Feng, Y., & Yang, S. L. (2022). Two new compounds from *Sabia parviflora*. *Chinese Traditional and Herbal Drugs, 53*(7), 1939–1942.

Zhou, S. Y., Chen, J., Liu, Z., Zhou, J., Liu, Y., Liu, S., ... Chen, C. (2021b). Research progress on chemical constituents and pharmacological effects of *Sophorae Tonkinensis Radix* et *Rhizoma*. *Chinese Traditional and Herbal Drugs, 52*(5), 1510–1521.

Zhou, W., Dong, M., Wu, H., Li, H., Xie, J., Ma, R., & Dai, J. (2021c). Common mechanism of *Citrus Grandis Exocarpium* in treatment of chronic obstructive pulmonary disease and lung cancer. *Chinese Herbal Medicines, 13*(4), 525–533.